Short communication

Diastereoselective intramolecular C–H bond activation on a prochiral sp3 carbon by a cationic Ir(I) complex having an optically active P–N hybrid ligand

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Abstract

Highly diastereoselective intramolecular C–H bond activation at a prochiral sp3 carbon was achieved with a cationic iridium complex having an optically active heterochelate PN*(R) [PN*(R) = o-Ph$_2$PC$_6$H$_4$CH$_2$OCH$_2$C=NCH(R)CH$_2$O] ligand.
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1. Introduction

Stereoselective cleavage of an inert C–H bond by transition metal complexes is a significant and atom-economical synthetic procedure. A practical and catalytic method for the asymmetric C–H bond activation via C–H insertion with rhodium carbenoid intermediates has been extensively developed and some excellent results have been provided [1]. Application of the traditional C–H bond activation via oxidative addition to asymmetric syntheses is a promising but still challenging project [2]. In order to establish this methodology, the development of the key process in which a transition metal complex having a chiral ligand activates one of the two diastereotopic C–H bonds selectively is indispensable [3–8]. Recently, Sames and coworkers [8a] succeeded in asymmetric C–H bond activation and successive functionalization (dehydrogenation) of the pro(R) alkyl group in the total synthesis of (−)-Rhazinilam, but no examples of direct stereoselective activation of one of the two C–H bonds attached to a pro-chiral sp3 carbon in a transition metal complex have been reported except for Togni's report [6]. We have been interested in C–H and C–O bond activation of Ir or Pt complexes using our PN ligand [9] and have demonstrated stereoselective C–H bond activation of the Ir complex having the PN/CH$_3$ ligand [9b]. Herein, we describe the diastereoselective prochiral C(sp3)–H bond activation of Ir complexes having our novel chiral P–N hemilabile ligand, PN*(R) **1** [10].

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a : R = Et (*R*)
b : R = ^{i}Pr (*S*)
c : R = Ph (*R*)

PN*(R) ligand (**1**)
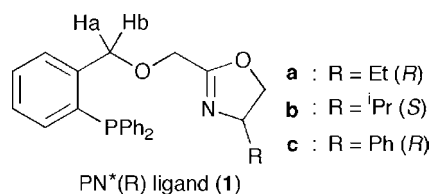
2. Results and discussion

The cationic Ir(I) complex [Ir(cod){(*R*)-PN*(Et)-*kP:kN* }]PF$_6$ (**2a**) was prepared by the reaction of [IrCl(cod)]$_2$ with two equiv of the (*R*)-PN*(Et) ligand **1a** in the presence of excess AgPF$_6$ in ethanol at room temperature for 5 h, which was a similar method to the preparation of the cationic Ir(I) complexes having the PN ligand previously reported by us (Eq. (1)) [9a]. An analytically pure complex of **2a** was precipitated directly from the reaction mixture as orange powders in good yield. The ^{31}P NMR spectrum in CDCl$_3$ showed that the complex **2a** was comprised of two isomers (**2a**-major:**2a**-minor = 84:16). Although we have not been able to succeed in X-ray analysis of **2a** so far, the spectral and physical data in addition to the information about our iridium complexes having the PN or PN/CH$_3$ ligand [9a,9b] indicated that the complex **2a** had a square pyramidal structure in which the oxygen in the (*R*)-PN*(Et) ligand co-ordinated to the Ir center weakly. Thus, the complex **2a** consisted of two diastereomers arising from a planar chirality around the square planar plane and the stereogenic center in the oxazoline ring.

(1)

2a
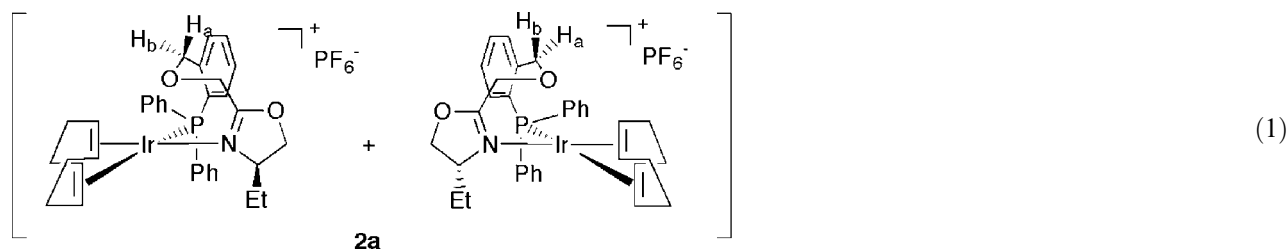
The complex **2a** was stable in the solid state, but on being dissolved in CD$_2$Cl$_2$, the color of the solution gradually changed from orange to pale yellow. The intramolecular C–H bond activation at the benzylic position of the (*R*)-PN*(Et) ligand easily occurred at 35 °C to give an Ir(III) hydrido alkyl complex **3a** as a mixture of two diastereomers (Eq. (2)). In the ^{31}P NMR spectrum of a CD$_2$Cl$_2$ solution of **2a**, two new signals appeared at 31.4 ppm for **3a**-major and at 26.2 ppm for **3a**-minor in addition to signals for **2a**-major and **2a**-minor, and no other products could be observed. A signal increase of **3a** and a decrease of **2a** were mutually correlated. The ratio of **3a**-minor reached the maximum point (ca. 10%) after 7 h and then decreased gradually. After 96 h, the composition of the four isomers became constant (**2a**-major:**2a**-minor:**3a**-major:**3a**-minor = 8:0:86:6). The ratio of the major isomers increased from 84% (**2a**-major) to 94% (the sum of **2a**-major and **3a**-major). When the pure isolated complex **3a**-major was dissolved in CD$_2$Cl$_2$, an equilibrium mixture of **2a** and **3a** was obtained again and its ratio finally reached the same value as above after 96 h (**2a**-major:**2a**-minor:**3a**-major:**3a**-minor = 8:0:86:6). These observations indicated that, besides the C–H bond activation and its reverse reductive elimination, isomerization between **2a**-major and **2a**-minor also proceeded to afford an equilibrium mixture of the four complexes.

(2)

3a-major   **3a**-minor
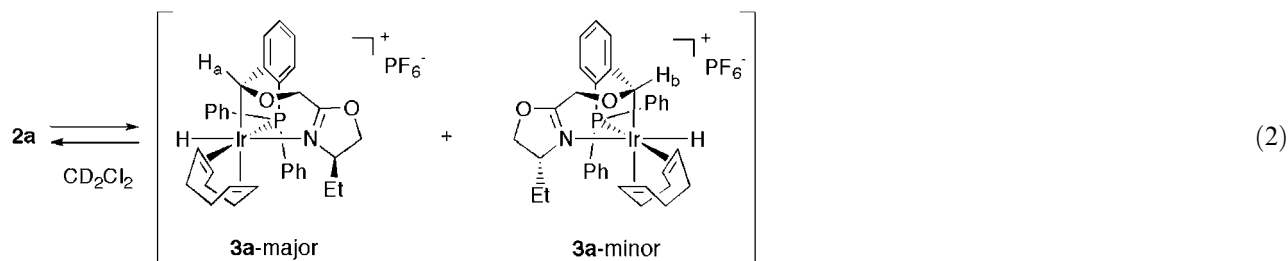
The structure of **3a**-major was confirmed by an X-ray analysis as well as the spectral data and the elemental analysis. The complex **3a**-major could be isolated as pale yellow crystals by recrystallization of the equilibrium mixture of **2a** and **3a** from a dichloromethane and hexanes solution. An ORTEP view is displayed in Fig. 1. The Ir(III) center exhibits a distorted octahedral geometry. The (*R*)-PN*(Et) ligand functions as a P–C–N tridentate ligand coordinated by
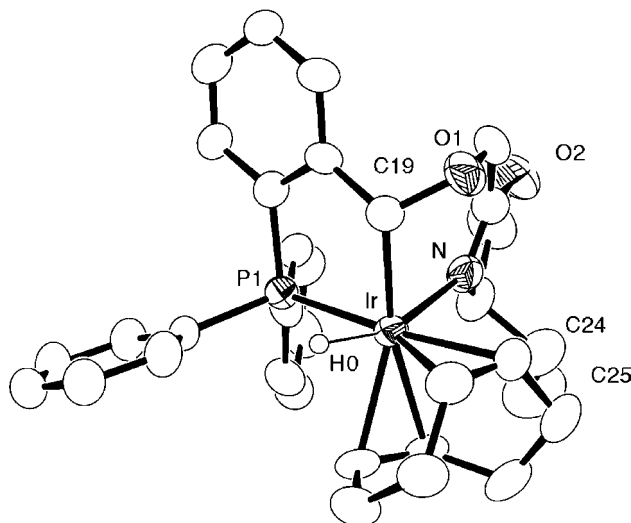
Fig. 1. The structure of the cationic part of **3a**-major, Hydrogen atoms except the hydride ligand are omitted for clarity and thermal ellipsoids are shown at the 50% probability level.

phosphorus, benzylic carbon (C19), and nitrogen atoms in a facial manner. A similar metal coordination system has been found in the Ir complexes having PCN or PCN/CH$_3$ ligands [9a,9b]. Since the absolute configuration of the stereogenic center in the oxazoline ring is *R*, that of the benzylic carbon (C19) attached to the Ir metal is *R*. The oxazoline ring and the diphenyl phosphino group coordinate to the Ir center in a *cis* configuration. In order to avoid steric hindrance, the Et group on the oxazoline ring faces the open space opposite to that occupied by one phenyl ring in the diphenyl phosphino group.

The ^{1}H NMR spectrum of **3a**-major was consistent with the structure determined by the X-ray analysis. Appearance of a singlet signal at δ 6.25 (1H) showed the presence of a proton attached to the benzylic carbon bound to the Ir center and that of a doublet signal at δ-17.92 ($J_{\text{P–H}}$ = 14.6 Hz, 1H) showed the presence of a metal hydride at the *cis* position of the phosphorus atom though it could not be detected by the X-ray analysis. Unfortunately, the structure of **3a**-minor could not be determined clearly from the ^{1}H NMR spectrum due to its peaks being concealed under those of **3a**-major, but **3a**-minor would be a stereoisomer of **3a**-major as described in Eq. (2). The steric repulsion between the phenyl ring and the ethyl group made **3a**-minor less stable kinetically and thermodynamically than **3a**-major. That is, the steric hindrance of the substituents causes the Ir(I) metal to discriminate the two prochiral C–H bonds, and then the Ir hydrido complex having an *R,R* configuration (**3a**-major) was obtained selectively.

When bulkier substituents in the oxazoline ring were used, excellent stereo-discrimination in the C–H bond activation was observed. The complex **2b** or **2c**, [Ir(cod){PN*(*R*)-*kP:kN*}]PF$_6$ {**2b**: *R* = $^{\text{i}}$Pr(*S*); **2c**: *R* = Ph(*R*)} was prepared from **1b** or **1c**, respectively, by a similar method to the preparation of **2a**. The ^{31}P NMR showed that the complex **2b** was a single diastereomer and the complex **2c** was comprised of two isomers (major:minor = 96:4). When the complex **2b** or **2c** was dissolved in CD$_2$Cl$_2$, the intramolecular C–H bond activation occurred and the corresponding Ir(III) hydrido complex **3b** or **3c** was obtained as a single diastereomer. The structure of **3b** was also confirmed by an X-ray analysis, indicating that the substituent in the oxazoline ring occupied the opposite side to that of a phenyl group of the diphenylphosphino group in the same way as the case of **2a**-major. Although each initial rate and activated Gibbus energy ($\Delta G^{\neq}$) were measured by UV visible spectrometry, no significant influence based on the electronic and the steric characters of the substituents in the oxazoline ring was observed [11]. The selectivity of the C–H bond activation was controlled by a difference in thermodynamic stability between the resulting Ir(III) hydrido complexes.

3. Experimental

3.1. Selected data for **2a**

Mp: 193.0 °C. ^{1}H NMR (CDCl$_3$, 270.05 MHz): δ 0.82 (t, *J* = 7.4 Hz, 3H, major), 1.44–1.84 (m, 3H, major), 1.95–2.35 (m, 4H, major), 2.23–2.60 (m, 3H, major), 3.00–3.21 (m, 1H, major), 3.0–5.2 (m, 4H, major), 3.46 (t, *J* = 8.9 Hz, 1H, major), 3.87 (t, *J* = 8.9 Hz, 1H, major), 4.29 (d, *J* = 14.8 Hz, 1H, major), 4.69 (d, *J* = 14.8 Hz, 1H, major), 4.81

(d, $J = 13.1$ Hz, 1H, major), 5.23 (d, $J = 13.1$ Hz, 1H, major), 6.78–7.02 (m, 3H, major), 7.19–7.88 (m, 9H, major), 7.81–8.02 (m, 2H, major). ^{31}P{^{1}H} NMR (CDCl$_3$): δ 11.0 (s, major), 13.9 (s, minor). Anal. Found: C, 46.55; H, 4.56; N, 1.65. Calcd. for C$_{33}$H$_{38}$F$_6$IrNO$_2$P$_2$: C, 46.70; H, 4.51; N, 1.65%.

3.2. Selected data for 3a

Mp: 162.1 °C (dec). ^{1}H NMR (CDCl$_3$, 399.65 MHz): δ 17.92 (d, $J = 14.6$ Hz, 1H, major), 0.81 (t, $J = 6.9$ Hz, 3H, major), 1.57–1.82 (m, 2H, major), 1.98–2.18 (m, 2H, major), 2.19–2.36 (m, 1H, major), 2.31 (t, $J = 8.6$ Hz, 1H, major), 2.51–2.76 (m, 3H, major), 3.11–3.21 (m, 1H, major), 3.22–3.33 (m, 1H, major), 3.34–3.43 (m, 1H, major), 3.80 (d, $J = 18.9$ Hz, 1H, major), 3.85 (dd, $J = 3.4, 8.6$ Hz, 1H, major), 4.07 (d, $J = 18.9$ Hz, 1H, major), 4.94–5.12 (m, 3H, major), 5.37–5.48 (m, 1H, major), 6.25 (s, 1H, major), 7.12 (t, $J = 7.7$ Hz, 1H, major), 7.28–7.39 (m, 3H, major), 7.42–7.56 (m, 6H, major), 7.64–7.74 (m, 4H, major). ^{31}P{^{1}H} NMR (CDCl$_3$): δ 31.4 (s, major), 26.2 (s, minor). Anal. Found: C, 46.23; H, 4.45; N, 1.96. Calcd. for C$_{33}$H$_{38}$F$_6$IrNO$_2$P$_2$: C, 46.70; H, 4.51; N, 1.65%.

3.3. Crystal data for 3a major

C$_{33}$H$_{36}$F$_6$IrNO$_2$P$_2$, $M = 848.78$, orthorhombic, $a = 14.713(5)$ Å, $b = 23.317(2)$ Å, $c = 9.452(4)$ Å, $U = 3243(2)$ Å^3, $T = 293(2)$ K, space group $P2_12_12_1$ (#19), $Z = 4$, μ(Mo-Kα) $= 4.282$ mm^{-1}, 4174 unique reflections were used in all calculations, absorption correction (psi-scan method, $T_{(min)} = 0.2090$, $T_{(max)} = 0.6517$). The structure was solved by direct methods (SHELXS-86) [12] and refined on F^2 by full-matrix least-squares methods, using SHELXL-97 [13]. Probable hydride atom positions were calculated at the minimum of potential energy by the program HYDEX [14] and were included as fixed contributions. R_1 and wR_2 are 0.0332 and 0.0762 for 3554 reflections with $I > 2.0\sigma(I)$, respectively. Final R factors, R_1 and wR_2 are 0.0523 and 0.0871 for all reflections respectively. Flack parameter (χ) shows $-0.021(13)$.

4. Supplementary materials

The X-ray crystallographic files, in CIF format, are available from the Cambridge Crystallographic Data Centre on quoting the deposition numbers: CCDC 205258. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: 44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk). Supporting characteristic data for the new compounds are available.

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[10] The (*R*) or (*S*)-PN*(*R*) ligand could be prepared from 2-(cyanomethoxymethyl)-phenyldiphenyl phosphine and (*R*) or (*S*)-2-subustituted aminoethanol [*R*(NH$_2$)CHCH$_2$OH] in the presence of ZnCl$_2$. The detailed procedure for the preparation of the ligand will be reported separately.

[11] **2a**: $k_{obs} = 5.14 \times 10^{-5}$ s^{-1}, $\Delta G^{\neq} = 9.91 \times 10^4$ J/mol. **2b**: $k_{obs} = 8.30 \times 10^{-5}$ s^{-1}, $\Delta G^{\neq} = 9.79 \times 10^4$ J/mol. **2c**: $k_{obs} = 5.12 \times 10^{-5}$ s^{-1}, $\Delta G^{\neq} = 9.91 \times 10^4$ J/mol.

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